Antiarrhythmias
Edward JN Ishac, Ph.D.
Smith Building, Room 742
eishac@vcu.edu
828-2127
Department of Pharmacology and Toxicology
Medical College of Virginia
Campus of Virginia Commonwealth University
Richmond, Virginia, USA

Agents used in HT, CHF, Arrhythmia and Angina

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Hypertension</th>
<th>CHF</th>
<th>Arrhythmia</th>
<th>Angina</th>
<th>Contraindications/Cautions/Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-Blockers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CHF (unstable CHF, bronchoospasm, significant bradycardia); or in diabetes, asthma (use β1-selective), depression, rebound HT</td>
</tr>
<tr>
<td>Ca++-Channel blockers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CHF, Gingival hyperplasia, reflex tachycardia, constipation</td>
</tr>
<tr>
<td>ACEI / ARBs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Low GFR, renal steatosis, glossitis, tetrademic, cough (ACEI); taste, Thrombo-mechanical, angioedema</td>
</tr>
<tr>
<td>Diuretics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Low GFR, hypokalemia → CG; glucose intolerance → diabetes</td>
</tr>
<tr>
<td>Cardiac glycosides</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Many Rx interactions, see β; [K+] important, low K+ → toxicity</td>
</tr>
<tr>
<td>Vasodilators</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flushing, dizienesa, headache, reflex tachycardia, combo Rx</td>
</tr>
<tr>
<td>Non-Channel blockers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Effects enhanced in depolarized tissue, damaged tissue. Phase 0</td>
</tr>
<tr>
<td>Nitrates</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heart Physiology
Closed system
Supply nutrients/O₂
Remove metabolites

Heart Physiology

P - atria depolarization
QRS - ventricle depolarization
PR - conduction A-V
T - ventricle repolarization
QT - duration ventricle of repolarization

Electrocardiogram (ECG)
**Ion Permeability**

<table>
<thead>
<tr>
<th>mM</th>
<th>Na⁺</th>
<th>K⁺</th>
<th>Ca²⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td>Out</td>
<td>140</td>
<td>4</td>
<td>2.5</td>
</tr>
<tr>
<td>In</td>
<td>10</td>
<td>150</td>
<td>0.1</td>
</tr>
</tbody>
</table>

**Cardiac Action Potentials**

**Ion Flow**

| 0  | Na⁺ - open |
| 1  | Na⁺ - close |
| 2  | Ca²⁺ - open |
| 3  | Ca²⁺ - close |
| 4  | K⁺ - close  |

Na⁺/Ca²⁺ - exchange (3:1)
Na⁺/K⁺ - ATPase (3:2)

---

**Characteristics of Arrhythmias**

**Definitions:**
- normal sinus rhythm (60-90bpm), SA node pacemaker
- arrhythmia; any abnormality of firing rate, regularity or site of origin of cardiac impulse or disturbance of conduction that alters the normal sequence of activity of atria and ventricles.

**Occurrence:**
- 80% of patients with acute myocardial infarctions
- 50% of anaesthetized patients
- about 25% of patients on digitalis

---

**Classification of arrhythmia**

1. **Characteristics:**
   a. flutter – very rapid but regular contractions
   b. tachycardia – increased rate
   c. bradycardia – decreased rate
   d. fibrillation – disorganized contractile activity

2. **Sites involved:**
   a. ventricular
   b. atrial
   c. sinus
   d. AV node
   e. Supraventricular (atrial myocardium or AV node)

---

**Examples of Arrhythmias**

---

**Mechanisms of arrhythmias**

1. **Abnormal impulse generation (abnormal automaticity)**
   a. automaticity of normally automatic cells (SA, AV, His)
   b. generation of impulses in normally non-automatic cells
   - development of phase 4 depolarization in normally non-automatic cells
   - ‘triggered activity’ due to afterdepolarizations
   - early afterdepolarization
   - delayed afterdepolarization

2. **Abnormal impulse conduction (more common mechanism)**
   a. AV block – ventricle free to start own pacemaker rhythm
   b. Re-entry: re-excitation around a conducting loop, which produces tachycardia
   - unidirectional conduction block
   - establishment of new loop of excitation
   - conduction time that outlasts refractory period
Heart Physiology

Closed system
Pressure driven
Supply nutrients/O₂
Remove metabolites

P - atria depol.
QRS - ventricle depol.
PR - conduction A-V
T - ventricle repol.
QT - duration
ventricle repolarization

Unidirectional Block

Damaged tissue is usually depolarized → ↓ conduction velocity

Strategy of Antidysrhythmic Agents

Suppression of dysrhythmias

A. Alter automaticity
   i. decrease slope of Phase 4 depolarization
   ii. increase the threshold potential
   iii. decrease resting (maximum diastolic) potential

B. Alter conduction velocity
   i. mainly via decrease rate of rise of Phase 0 upstroke
   ii. decrease Phase 4 slope
   iii. decrease membrane resting potential and responsiveness

C. Alter the refractory period
   i. increase Phase 2 plateau
   ii. increase Phase 3 repolarization
   iii. increase action potential duration

Classification of Antidysrhythmic Drugs

Vaughan-Williams classification (1970), subsequently modified by Harrison.

Helpful, But?

1. based on electrophysiological actions in normal tissue
2. presumes a mechanism of action of antidysrhythmic drugs
3. consists of four main classes and three subclasses
4. does not include actions of other agents (ie. adenosine)

### Vaughan-Williams Classification

<table>
<thead>
<tr>
<th>Subclass</th>
<th>Mechanism</th>
<th>Prototype</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Moderate block Ph.0; slow conduction; ↑ APD</td>
<td>Quinidine, Procainamide</td>
</tr>
<tr>
<td>IB</td>
<td>Minimal block Ph.0; slow conduction (less); shorten Ph.3 repolarization</td>
<td>Lidocaine, Phenytoin</td>
</tr>
<tr>
<td>IC</td>
<td>Marked block Ph.0; slow conduction; no change APD or repolarization. Increased suppression of Na channels</td>
<td>Flecainide, Encainide</td>
</tr>
<tr>
<td>Class II</td>
<td>Beta blockers; decrease adrenergic input. No major effect on APD, suppress Ph.4 depolarization</td>
<td>Propranolol, others</td>
</tr>
<tr>
<td>Class III</td>
<td>Prolong repolarization/refractory period other means than exclusively Na block (mainly K⁺ channel blockade).</td>
<td>Amiodarone, Bretylium</td>
</tr>
<tr>
<td>Class IV</td>
<td>Ca channel blockers. Slow conduction and ↑ effective refractory period in normal tissue (A-V node) and Ca-dependent slow responses of depolarized tissue (atria, ventricle, Purkinje)</td>
<td>Verapamil, Diltiazem</td>
</tr>
<tr>
<td>Others</td>
<td>Adenosine, Digoxin, Anticoagulants, ANS agents</td>
<td></td>
</tr>
</tbody>
</table>

### Action Potential – Ion Flow

<table>
<thead>
<tr>
<th>mM</th>
<th>Na⁺</th>
<th>K⁺</th>
<th>Ca++</th>
</tr>
</thead>
<tbody>
<tr>
<td>Out</td>
<td>140</td>
<td>4</td>
<td>2.5</td>
</tr>
<tr>
<td>In</td>
<td>10</td>
<td>150</td>
<td>0.1</td>
</tr>
</tbody>
</table>

0 Na⁺ - open
1 Na⁺ - close
K⁺ - open/close
2 Ca⁺⁺ - open
K⁺ - leak
3 Ca⁺⁺ - close
K⁺ - open
4 K⁺ - close

Na⁺/Ca⁺⁺ - exchange (3:1)
Na⁺/K⁺ - ATPase (3:2)
### Electrophysiological Properties Of Specialized Cardiac Fibers

<table>
<thead>
<tr>
<th>Class of Antiarrhythmic Drug</th>
<th>Class IA</th>
<th>Class IB</th>
<th>Class IC</th>
<th>Class III</th>
<th>Class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>AV node</td>
<td>↓, ↑</td>
<td></td>
<td></td>
<td>↓, ↑</td>
<td>↓, ↑</td>
</tr>
<tr>
<td>Effective refractory period (ERP)</td>
<td>↑, ↓</td>
<td>↓, ↑</td>
<td>↓, ↑</td>
<td>↓, ↑, ↑</td>
<td>↓, ↑</td>
</tr>
<tr>
<td>Purkinje fibers</td>
<td>↓, ↓</td>
<td>↓, ↑</td>
<td>↓, ↑</td>
<td>↓, ↑</td>
<td>↓, ↑</td>
</tr>
<tr>
<td>Action potential duration (APD)</td>
<td>↓, ↑</td>
<td>↓, ↑</td>
<td>↓, ↑</td>
<td>↓, ↑</td>
<td>↓, ↑</td>
</tr>
<tr>
<td>Effective refractory period (ERP)</td>
<td>↑, ↓</td>
<td>↓, ↑</td>
<td>↓, ↑</td>
<td>↓, ↑</td>
<td>↓, ↑</td>
</tr>
<tr>
<td>ERI/APD</td>
<td>↑, ↓</td>
<td>↑, ↓</td>
<td>↑, ↓</td>
<td>↑, ↓</td>
<td>↑, ↓</td>
</tr>
<tr>
<td>Membrane responsiveness</td>
<td>↓, 0</td>
<td>↓, ↓</td>
<td>↓, ↓</td>
<td>↓, ↓</td>
<td>↓, 0</td>
</tr>
<tr>
<td>Automaticity</td>
<td>↓, 0</td>
<td>↓, ↓</td>
<td>↓, ↓</td>
<td>↓, 0</td>
<td>↓, 0</td>
</tr>
</tbody>
</table>

### Quinidine (Class IA prototype)

Other examples: Procainamide, Disopyrimide

1. **General properties:**
   a. D-isomer of quinine
   b. As with most of the Class I agents
      - moderate block of sodium channels
      - decreases automaticity of pacemaker cells
      - increases effective refractory period/AP duration

### Actions of Quinidine

**Cardiac effects**
- ↓ automaticity, conduction velocity and excitability of cardiac cells.
- Preferentially blocks open Na channels
- Recovery from block slow in depolarized tissue; lengthens refractory period (RP)
- All effects are potentiated in depolarized tissues
- Increases action potential duration (APD) and prolongs AP repolarization via block of K channels; decreases reentry
- Indirect action: anticholinergic effect (accelerates heart), which can speed A-V conduction.

### Actions & Toxicity of Quinidine

**Extracardiac**
- Blocks alpha-adrenoreceptors to yield vasodilatation.
- Other strong antimuscarinic actions

**Toxicity**
- "Quinidine syncope" (fainting)- due to disorganized ventricular tachycardia
- Associated with greatly lengthened Q-T interval; can lead to Torsades de Pointes (precursor to ventricular fibrillation)
- Negative inotropic action (decreases contractility)
- GI - diarrhea, nausea, vomiting
- CNS effects - headaches, dizziness, tinnitus (quinidine "Cinchonism")

### Quinidine: Pharmacokinetics/therapeutics

a. Oral, rapidly absorbed, 80% bound to membrane proteins
b. Hydroxylated in liver; T½ = 6-8 h
c. Drug interaction: displaces digoxin from binding sites; so avoid giving drugs together
d. Probably are active metabolites of quinidine
e. Effective in treatment of nearly all dysrhythmias, including:
   1) Premature atrial contractions
   2) Paroxysmal atrial fibrillation and flutter
   3) Intra-atrial and A-V nodal reentrant dysrhythmias
   4) Wolff-Parkinson-White tachycardias (A-V bypass)
f. Especially useful in treating chronic dysrhythmias requiring outpatient treatment

### Procainamide (Class 1A)

**Cardiac effects**
- Similar to quinidine, less muscarinic & alpha-adrenergic blockade
- Has negative inotropic action also

**Extracardiac effects**
- Ganglionic blocking reduces peripheral vascular resistance

**Toxicity**
- Cardiac: Similar to quinine; cardiac depression
- Noncardiac: Syndrome resembling lupus erythematosus

**Pharmacokinetics/therapeutics**
- Administered orally, i-v and intramuscularly
- Major metabolite in liver is N-acetylprocainamide (NAPA), a weak Na channel blocker with class III activity. Bimodal distribution in population of rapid acetylators, who can accumulate high levels of NAPA.
- T½ = 3-4 hours; necessitates frequent dosing; kidney chief elimination path. NAPA has longer T½ and can accumulate
- Usually used short-term. Commonly used in CCUs for ventricular dysrhythmias associated with acute myocardial infarctions (MI)
**Lidocaine (Class IB prototype)**

Other examples: Mexiletine, Phenytoin, Tocainide

**General**
- Commonly used antidysrhythmic agent in emergency care (decreasing use)
- Given i-v and i-m; widely used in ICU-critical care units (old DOC, prior 2001)
- Low toxicity
- A local anesthetic, works on nerve at higher doses

**Lidocaine Actions**

**Cardiac effects**
- Generally decreases APD, hastens AP repolarization, decreases automaticity and increases refractory period in depolarized cells.
- Exclusively acts on Na channels in depolarized tissue by blocking open and inactivated Na channels
- Potent suppresser of abnormal activity
- Most Na channels of normal cells rapidly unblock from lidocaine during diastole; few electrophysiological effects in normal tissue

**Toxicity:**
- Least cardiotoxic, high dose can lead to hypotension
- Tremors, nausea, slurred speech, convulsions

**Pharmacokinetics/therapy**
- i-v, i-m since extensive first pass hepatic metabolism
- T1/2 = 0.5-4 hours
- Effective in suppressing dysrhythmia associated with depol. tissue (ischemia; digitalis toxicity); ineffective against dysrhythmias in normal tissue (atrial flutter).
- Suppresses ventricular tachycardia; prevents fibrillation after acute MI; rarely used in supraventricular arrhythmias

---

**Phenytoin (Class IB)**

1. Non-sedative anticonvulsant used in treating epilepsy ('Dilantin')
2. Limited efficacy as antidysrhythmic (second line antiarrhythmic)
3. Suppresses ectopic activation by blocking Na and Ca channels
4. Especially effective against digitalis-induced dysrhythmias
5. T1/2 = 24 hr - metabolized in liver
6. Gingival hyperplasia (40%)

---

**Flecainide (Class IC prototype)**

Other examples: Lorcainide, Propafenone, Indecainide, Moricizine

Depress rate of rise of AP without change in refractoriness or APD in normally polarized cells
1. Decreases APD, decreases automaticity, conduction in depolarized cells.
2. Marked block of open Na channels (decreases Ph. 0); no change repolarization.
3. Used primarily for ventricular dysrhythmias but effective for atrial too
4. No antimuscarinic action
5. Suppresses premature ventricular contractions
6. Associated with significant mortality; thus, use limited to last resort applications like treating ventricular tachycardias

---

**Gingival Hyperplasia**

- Phenytoin (Dilantin) – anticonvulsant (40%)
- Calcium blockers – especially nifedipine (<10%)
- Cyclosporine – immunosuppressant (30%)

---

**Propranolol (Class II, beta adrenoreceptor blockers)**

Other agents: Metoprolol, Esmolol (short acting), Sotalol (also Class III), Acebutolol

- Slow A-V conduction
- Prolong A-V refractory period
- Blocks A-V nodal reentrant tachycardia; inhibits ectopic foci
- Propranolol used to treat supraventricular tachydysrhythmias
- Contraindicated in ventricular failure; also can lead to A-V block.

Oral (propranolol) or IV. Extensive metabolism in liver.
Cardiac Action Potentials
Ion Flow

<table>
<thead>
<tr>
<th>mM</th>
<th>Na⁺</th>
<th>K⁺</th>
<th>Ca²⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td>Out</td>
<td>140</td>
<td>4</td>
<td>2.5</td>
</tr>
<tr>
<td>In</td>
<td>150</td>
<td>10</td>
<td>0.1</td>
</tr>
</tbody>
</table>

0 Na⁺ - open
1 Na⁺ - close K⁺o - open/close
2 Ca²⁺ - open K⁺o - leak
3 Ca²⁺ - close K⁺o - open
4 K⁺ - close

Na⁺/Ca²⁺ - exchange (3:1) Na⁺/K⁺ - ATPase (3:2)

Clinical uses: Beta-Blockers

- Angina (non-selective or β₁-selective)
  - Cardiac: VO₂ demand more than O₂ supply
  - Exercise tolerance ↑ in angina patients

- Arrhythmia (β₁-selective, LA-action)
  - β catecholamine-induced increases in conductivity and automaticity

- Congestive Heart Failure
  - caution with use

- Glaucma (non-selective)
  - ↓ aqueous humor formation (Timolol)

- Other
  - block of tremor of peripheral origin (β₂-AR in skeletal muscle)
  - migraine prophylaxis (mechanism unknown)
  - hyperthyroidism: cardiac manifestation (only propranolol)
  - panic attacks, stage fright

β-Blockers: Untoward Effects, Contraindications

- Supersensitivity:
  - Rebound effect with β-blockers, less with β₁-blockers with partial agonist activity (ie. pindolol). Gradual withdrawal

- Asthma:
  - Blockade of pulmonary β₂-receptors increase in airway resistance (bronchospasm)

- Diabetes:
  - Compensatory hyperglycemic effect of EPI in insulin-induced hypoglycemia is removed by block of β₂-ARs in liver. β₁-selective agents preferred

Amiodarone (Class III)

General
- New DOC for ventricular dysrhythmias (Lidocaine, old DOC)
- prolongs refractory period by blocking potassium channels
- also member of Classes IA,II,III,IV since blocks Na, K, Ca channels and alpha and beta adrenergic receptors
- serious side effects (cardiac depression, pulmonary fibrosis)
- effective against atrial, A-V and ventricular dysrhythmias
- very long acting (>25 d)

Bretylium (Class III, K⁺ channel blockers)

Others Amiodarone, Ibutilide, (Sotalol, also beta-blocker)

General: originally used as an antihypertensive agent

Cardiac effects
- Direct antidysrhythmic action
- Increases ventricular APD and increases refractory period; decreases automaticity
- Most pronounced action in ischemic cells having short APD
- Initially stimulates and then blocks neuronal catecholamine release from adrenergic nerve terminals
- Blocks cardiac K channels to increase APD

Extraclardiac effects:
- Hypotension (from block of NE release)

Pharmacokinetics/therapeutics
- iv or intramuscular
- Excreted mainly by the kidney
- Usually for emergency use only: ventricular fibrillation when lidocaine and cardioversion therapy fail. Increases threshold for fibrillation.
- Decreases tachycardias and early extrasystoles by increasing effective refractory period
Verapamil (Class IV, Ca++ channel blockers)

Other example: Diltiazem - Increasing use and importance
a. Blocks active and inactivated Ca channels, prevents Ca entry
b. More effective on depolarized tissue, tissue firing frequently or areas where activity dependent on Ca channels (SA node; A-V node)
c. Increases A-V conduction time and refractory period; directly slows SA and A-V node automaticity
d. suppresses oscillatory depolarizing after depolarizations due to digitalis

Ca++ Channel Blockers - Actions

Extracardiac
a. Peripheral vasodilatation via effect on smooth muscle
b. Used as antianginal / antihypertensive
c. Hypotension may increase HR reflexively

Toxicity
a. Cardiac
  - Too negative inotropic for damaged heart, depresses contractility
  - Can produce full A-V block
b. Extracardiac
  - Hypotension
  - Constipation, nervousness
  - Gingival hyperplasia

Pharmacokinetics/Therapeutics
a. $T_{1/2} = 7h$, metabolized by liver
b. Oral administration; also available parenterally
c. Great caution for patients with liver disease
d. Blocks reentrant supraventriculartachycardia ("A-V nodal reentrant tachycardia"), decreases atrial flutter and fibrillation
e. Only moderately effective against ventricular arrhythmias

Dysrhythmics - Others

1. Adenosine: i.v. (secs), activates P1 purinergic receptors (A1) coupled to K channels, ↓ CV, ↑ refractory period
2. Potassium ions (K+): Depress ectopic pacemakers
3. Digoxin: used to treat atrial flutter and fibrillation
   - AV node ↓ conduction (vagal stimulation)
   - Purkinje fibers ↑ refractory period, ↓ conduction
4. Autonomic agents: used to treat A-V block
   - β-agonists, anticholinergics (ie. atropine)
5. Anticoagulant therapy: prevent formation of systemic emboli & stroke

Pharmacokinetic Properties of Antiarrhythmic Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Class</th>
<th>Plasma Binding %</th>
<th>$T_{1/2}$ (hrs)</th>
<th>Drug Excretion Unchanged</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quinidine</td>
<td>IA</td>
<td>60</td>
<td>5</td>
<td>20-40%</td>
</tr>
<tr>
<td>Procainamide</td>
<td>IA</td>
<td>15</td>
<td>4</td>
<td>80%</td>
</tr>
<tr>
<td>Disopyramide</td>
<td>IA</td>
<td>35-50</td>
<td>5</td>
<td>95-70%</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>IB</td>
<td>40</td>
<td>2</td>
<td>&lt;15%</td>
</tr>
<tr>
<td>Tacrinide</td>
<td>IB</td>
<td>10</td>
<td>14</td>
<td>40%</td>
</tr>
<tr>
<td>Mexiletine</td>
<td>IB</td>
<td>65</td>
<td>12</td>
<td>10%</td>
</tr>
<tr>
<td>Flecainide</td>
<td>IC</td>
<td>45</td>
<td>15</td>
<td>40%</td>
</tr>
<tr>
<td>Propranolol</td>
<td>II</td>
<td>90</td>
<td>4</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Acebutolol</td>
<td>II</td>
<td>25</td>
<td>4</td>
<td>40%</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>II</td>
<td>[hydro. esterase]</td>
<td>9 min</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Sotalol</td>
<td>III</td>
<td>9</td>
<td>90%</td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td>III</td>
<td>95</td>
<td>&gt; 25 days</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Bretylium</td>
<td>III</td>
<td>5</td>
<td>9</td>
<td>80%</td>
</tr>
<tr>
<td>Verapamil</td>
<td>IV</td>
<td>90</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Adenosine</td>
<td>Misc (other)</td>
<td>15 sec</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Cardiac Effects of Antiarrhythmic Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Class</th>
<th>Auto</th>
<th>CV</th>
<th>RP</th>
<th>APD</th>
<th>ANS effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disopyramide</td>
<td>IA</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>vagal, β-block</td>
</tr>
<tr>
<td>Procainamide</td>
<td>IA</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>vagal, α-block</td>
</tr>
<tr>
<td>Disopyramide</td>
<td>IA</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>vagal, α-block</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>IB</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Tacrinide</td>
<td>IB</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mexiletine</td>
<td>IB</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Flecainide</td>
<td>IC</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Propranolol</td>
<td>II</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>β-block</td>
</tr>
<tr>
<td>Acebutolol</td>
<td>II</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>β-block</td>
</tr>
<tr>
<td>Sotalol</td>
<td>III</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>β-block</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>III</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>α, β-block</td>
</tr>
<tr>
<td>Bretylium</td>
<td>III</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>Sympatholytic</td>
</tr>
<tr>
<td>Verapamil</td>
<td>IV</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>vagal stimulation</td>
</tr>
</tbody>
</table>

More important agents